Left Ventricular Rapid Pacing Via the Valve Delivery Guidewire in Transcatheter Aortic Valve Implantation

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Tweet/handle: faurieb@gmail.com: Discover the first randomized trial comparing standard RV stimulation to direct wire pacing via the LV backup wire. This disruptive technique optimize TAVR procedures (reducing costs, procedural and scopy time) while maintaining safety and efficacy!
ABSTRACT
Background: Rapid ventricular pacing is necessary to ensure cardiac standstill during transcatheter aortic valve implantation (TAVI).
Objectives: We investigated whether left ventricular (LV)-stimulation via a guidewire reduced procedure duration while maintaining efficacy and safety compared with standard right ventricular (RV)-stimulation.
Methods: This is a prospective, multicenter, single-blinded, superiority, randomized controlled trial. Patients undergoing transfemoral TAVI with a Sapien valve (Edwards Lifesciences) were allocated to LV- or RV-stimulation. The primary endpoint was procedure duration. Secondary endpoints included efficacy, safety, and cost at 30 days. This trial is registered at clinicaltrials.gov (NCT02781896).
Results: Between May 2017 and May 2018, 307 patients were randomised but 4 were excluded because they did not receive the intended treatment: 303 patients were analysed in the LV- (n=151) or RV-stimulation (n=152) groups. Mean procedure duration was significantly shorter in the LV-stimulation group (48.4±16.9 vs. 55.6±26.9 min, p=0.0013), with a difference of -0.12 (95% CI -0.20 to -0.05) in the log transformed procedure duration (p=0.0012). Effective stimulation was similar in the LV- and RV-stimulation groups: 124 (84.9%) vs. 128 (87.1%), p=0.60. Safety of stimulation was also similar in the LV- and RV-stimulation groups: procedural success occurred in 151 (100%) vs. 151 (99.3%) patients (p=0.99); 30-day MACE-TAVI occurred in 21 (13.9%) vs. 26 (17.1%) patients (p=0.44); fluoroscopy time was lower in the LV-stimulation group (13.48±5.98 vs. 14.60±5.59, p=0.02) as was cost (€18,807±1,318 vs. €19,437±2,318, p=0.001).
Conclusions: Compared with RV-stimulation, LV-stimulation during TAVI was associated with significantly reduced procedure duration, fluoroscopy time, and cost, with similar efficacy and safety.

KEY WORDS: left-ventricular stimulation, left-ventricular pacing, transcatheter aortic valve implantation, transcatheter aortic valve replacement

CONDENSED ABSTRACT
The EASY-TAVI randomized trial (n=303) compared left ventricular (LV)-stimulation via a guidewire with standard right ventricular (RV)-stimulation for rapid ventricular pacing during TAVI with a SAPIEN 3 valve. The primary endpoint was procedure duration. LV-stimulation significantly reduced procedure duration (48.4±16.9 vs. 55.6±26.9 min, p=0.0013), fluoroscopy time (13.48±5.98 vs. 14.60±5.59, p=0.02), and cost (€18,807±1,318 vs. €19,437±2,318, p=0.001) compared with RV-stimulation, while maintaining efficacy and safety. By eliminating the need for a transvenous temporary pacing lead or additional venous access in most cases, LV-stimulation succeeded in simplifying the TAVI procedure and should be considered as the default strategy for rapid ventricular pacing.

ABBREVIATIONS AND ACRONYMMS
LV: left ventricular
RV: right ventricular
TAVI: transcatheter aortic valve implantation
INTRODUCTION

Since the introduction of transcatheter aortic valve implantation (TAVI) in 2002, the procedure has undergone considerable refinement, owing to improved operator experience, patient-selection, and pre-procedural imaging, as well as advances in device technologies. Such improvements have resulted in reduced procedural complication rates and improved patient outcomes.(1-4) Refinements of the TAVI procedure have included simplification of the technique, to reduce procedure duration and fluoroscopy time, and a more minimalistic approach, to reduce procedural complications. Such measures include increased use of conscious sedation rather than general anaesthesia; increased use of transfemoral rather than alternative access routes, using lower profile vascular access sheaths; radial rather than contralateral femoral access as secondary access; and reduced use of predilatation.(5)

Despite such advances, intraprocedural rapid ventricular pacing is still necessary to ensure transient cardiac standstill during valve positioning and deployment, as well as during pre- and post-dilatation, when performed. This is typically achieved using a transvenous temporary pacing lead, advanced to the right ventricular apex, usually under fluoroscopy. This requires additional venous access, with the inherent risk of vascular complications, including bleeding, pseudoaneurysm, arterio-venous fistula, thrombosis, or infection. In addition, the temporary pacing lead carries the risk of right ventricular perforation, with pericardial effusion or life-threatening cardiac tamponade. Use of a right ventricular pacing lead also adds to procedure duration, fluoroscopy use, and cost. Moreover, lead instability in the right ventricle can result in loss of capture and valve embolization.

With this in mind, a technique of rapid ventricular pacing through the left ventricular guidewire used for balloon advancement during pediatric balloon aortic valvuloplasty was previously developed to obviate the need for a temporary pacing lead.(6,7) The safety and efficacy of this technique during TAVI has recently been demonstrated.(8,9) Against this
background, the aim of the current study is to investigate whether left ventricular (LV)-
stimulation using the valve delivery guidewire reduces procedure duration compared with
right ventricular (RV)-stimulation using a standard temporary pacing lead, while maintaining
safety and efficacy during TAVI.

METHODS

Patients and study design

The EASY-TAVI trial is a prospective, multicentre, single-blinded, superiority, randomized
controlled trial. Patients aged \( \geq 18 \) years undergoing TAVI implantation with planned
transfemoral approach using the SAPIEN 3 or XT (Edwards Lifesciences, Irvine, CA, USA)
valve were eligible for inclusion. Patients undergoing TAVI with a planned access route
other than femoral or previous enrolment in this trial or another trial that might result in a
protocol deviation in either study were excluded. Written informed consent was obtained
from all patients or their legal representative. Patients were enrolled at ten centers in France
between May 2017 and May 2018; participating centers are listed in the online appendix. The
study was conducted in accordance with the provisions of the Declaration of Helsinki and
with the International Conference on Harmonization Good Clinical Practices and the
provisions established by the European Directives in March 2006 and November 2006
concerning the application of GCP. Ethical approval of the trial protocol was obtained from
the South-east V Committee for the Protection of Persons (CPP Sud-est V) and the National
Agency for the Safety of Medicines and Health Products (ANSM) in France. The trial was
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supervision, monitoring, data management and statistical analysis (other than the cost
analysis) were performed by CERC, Massy, France. The cost-analysis was done by Isabelle
Durand-Zaleski and colleagues at the Clinical research unit in health economics (URC ECO),
Île-de-France, Paris, France. This trial is registered at clinicaltrials.gov (NCT02781896). The trial is reported in line with CONSORT (Consolidated Standards of Reporting Trials) recommendations for reporting of randomized trials and a CONSORT checklist is included in the online appendix.

**Randomization and masking**

Patients who met all inclusion criteria and no exclusion criteria were randomized in the order that they qualified. Patients were randomly allocated (1:1) to TAVI with either LV- or RV-stimulation prior to the TAVI procedure. Each patient was assigned a unique identification number which was automatically generated by the electronic case report form (eCRF). Allocation to treatment was performed via the eCRF, by means of a computer-generated random sequence with block randomization and the allocation notification was sent via an automatically generated email. Patients were blinded to treatment allocation.

**Description of the experimental procedure**

Details of the experimental procedure (rapid left ventricular pacing via the valve delivery guidewire) have previously been described.\(^8\) In brief, in both treatment groups, transfemoral TAVI was carried out according to standard techniques but no systematic femoral vein puncture was performed for placement of a RV temporary pacemaker lead in the experimental group. Surgical femoral access was permitted. The second arterial sheath was placed either in the contralateral femoral artery or a radial artery according to operator preference.

In the experimental group, rapid ventricular pacing was provided via the 0.035-inch stiff guidewire placed in the left ventricle for valve advancement, with the transcatheter heart valve delivery system providing the required insulation. The cathode of an external pacemaker was attached to the distal external end of the guidewire using a crocodile clip. The anode (second crocodile clip) was attached to the incised skin at the insertion site of the
arterial sheath in the anesthetized groin (shown in Online figure 1). Efficacy of stimulation was tested during predilatation or before valve deployment with the transcatheter heart valve delivery system positioned in the ascending aorta above the aortic valve. During valve deployment, electric stimulation was delivered in asynchronous mode at an amplitude of 5 to 15 mA (at the discretion of the operator) and a rate of 160 to 220 bpm using a standard external pacemaker in order to achieve a decrease in systolic pressure ≤ 60 mmHg without loss-of-capture for at least 30 seconds (shown in Online figure 2). In the event of a complete atrio-ventricular block during the procedure, immediate stimulation was delivered through the LV guidewire while a venous sheath was inserted for RV temporary pacing lead placement and permanent pacemaker implantation was carried out within the next 24 hours, if required.

In the control group (rapid right ventricular pacing via a standard temporary pacing lead), the temporary pacing lead was inserted through a dedicated standard or long sheath inserted in the femoral vein. Use of a 5 or 6 french standard or balloon pacing catheter was permitted. The type, brand and size were left to the discretion of the operator. In the absence of a conduction disturbance requiring temporary pacing, the RV pacing lead was removed at the end of the procedure.

The choice of guidewire for valve delivery in both groups was restricted to four guidewires (Safari² large, small or extra small curve [Boston Scientific, Marlborough, MA, USA]; Amplatz Super Stiff, standard straight tip [Boston Scientific, Marlborough, MA, USA]; Amplatz Extra Stiff, curved tip [Cook Medical, Bloomington, IN, USA]; or Confida Brecker Curve [Medtronic, Minneapolis, MN, USA]) and was at the discretion of the individual operator.

**Endpoints**

The primary endpoint was procedure duration, defined as the time from first vascular puncture until withdrawal of the last vascular access sheath. Secondary endpoints included
efficacy and safety of pacemaker stimulation, other major cardiovascular events, length of hospital-stay, and cost at 30 days. Efficacy of pacemaker stimulation was defined as achievement and maintenance of a systolic blood pressure $\leq 60$ mmHg for more than 30 seconds without loss-of-capture. Safety of pacemaker stimulation was characterized by a combination of (i) procedural success (defined as absence of procedural mortality; correct positioning of the valve bioprosthesis in the targeted anatomical location; good post-procedural function of the valve bioprosthesis [trans valvular aortic gradient $<20$ mmHg]; and absence of severe regurgitation in the valve bioprosthesis post-procedure), (ii) procedural radiation exposure (assessed by cumulative fluoroscopy time, absorbed radiation dose (Air Kerma), and dose area product), and (iii) major adverse clinical and cerebrovascular events. MACE-TAVI was defined as a composite of all-cause mortality, major cerebrovascular events, myocardial infarction, cardiac tamponade, bleeding events, and vascular complications. Cardiovascular mortality was defined as any death due to an immediate cardiac cause (e.g. myocardial infarction, heart failure, fatal arrhythmia), unwitnessed death or death of unknown cause. Myocardial infarction and vascular complications were defined by VARC-2 criteria.(10) Bleeding events were defined by BARC criteria.(11) Study endpoint definitions are shown in Online table 1. Clinical outcomes were assessed immediately post-procedure, in-hospital, and at 30-day follow-up. Clinical follow-up at 30 days was by means of a telephone call. Patients also underwent echocardiography by the treating cardiologist at 30 days post-procedure and the report was obtained by study personnel. Clinical events were adjudicated and classified by an independent event adjudication committee blinded to treatment allocation (CERC).

Estimation of resources used and unit costs

The cost-effectiveness analysis took direct costs into account, including the cost of material for ventricular pacing and costs associated with the procedure (e.g., hospital stay)
and complications. Hospital resources included hospitalizations for the index procedure and re-hospitalizations within 30 days. We assumed that all major complications would result in re-hospitalization, and consequently, that out-of-hospital costs such as consultations, laboratory tests, imaging, and medications would be identical in both groups. The cost of the procedure for each patient was estimated using a micro-costing method and the cost of hospitalization was estimated based on bed days depending on the location (intensive or cardiac care unit or cardiology ward) and length of stay. The cost of hospitalization was estimated based on bed days depending on the location (intensive or cardiac care unit or cardiology ward) and length of stay.(12) Procedural costs were calculated based on the materials used during the procedure and the procedure duration. Repeat admissions were added when at least one concurrent adjudicated cardiac clinical endpoint was recorded on the same date. Severity-adjusted diagnosis related groups (DRG) for re-hospitalizations were assigned based on the primary indication for hospitalization, according to the DRG classification in France (Manuel des GHM - Version 11d for France). Hospital costs were also valued using DRG costs. All costs were in 2018 Euro.

**Sample size determination and statistical analysis**

We assumed a mean procedure duration of 80 ± 35 minutes for the control intervention (TAVI with RV-stimulation),(13-15) and a 12.5% reduction with the experimental technique (TAVI with LV-stimulation) to 70 ± 35 minutes.(8) As procedure duration follows a log-normal law, we relied on the properties of the normal law applied to the logarithm of the data for the calculation of the study sample size. Applying classical formulae,(16) the mean of the transformed time (transformation ln) would be 4.29 (with a standard deviation [SD] of 0.42) in the RV-stimulation group (control group) versus 4.14 (with a SD of 0.47) in the LV-stimulation group (experimental group). The number of subjects required to provide 80% power to detect this reduction at a two-sided α-error level of 5% is 126 per group (two group t-test of equal means [unequal variances], nQuery Advisor version 7.0, Cork, Ireland). Taking into account potential loss to follow-up, it was planned to
include 300 patients (150 patients in each group). For the primary outcome, missing data was
replaced by multiple imputation methods.

Categorical data are presented as counts or proportions (%). Continuous data are
presented as mean ± SD or median (interquartile range). Data distribution was tested for
normality using the Shapiro-Wilk test in addition to histograms. Differences between the
groups were assessed using the chi-square test or Fisher’s exact test for categorical data and
the Student t-test or Mann-Whitney-Wilcoxon test for continuous data. Crude clinical event
rates are shown at 30 days. Statistical analysis was modified intention-to-treat: patients who
did not receive the allocated treatment after randomization were excluded. The trial profile is
shown in Figure 1. A 2-sided p-value <0.05 was considered to indicate statistical
significance. Statistical and methodological analysis was supported by a biostatistician. SAS
version 9.4 was used for the statistical analysis. BF and TL had full access to all the data in
the study and had final responsibility for the decision to submit for publication.

Role of the funding source

The study sponsors had no role in study design, in the collection, analysis and
interpretation of data; in the writing of the report; or in the decision to submit the paper for
publication.

RESULTS

Between May 2017 and May 2018, 307 patients underwent randomization, four of whom
were excluded because three received a valve other than Sapien 3 or XT and one did not
undergo TAVI. The remaining 303 patients were included in the modified intention to treat
analysis: 151 in the LV-stimulation group and 152 in the RV-stimulation group (Figure 1).
There was no crossover between treatment groups. There were no significant differences
between treatment groups with respect to baseline demographic or clinical characteristics.
The mean logistic Euroscore was 12.99% and the mean STS score was 4.84%. Baseline
clinical characteristics are shown in Table 1 and additional characteristics are shown in Online table 2. The types of stiff left ventricular guidewire for valve delivery used in both groups are shown in Online table 3. Predilatation prior to valve implantation was done in 14 (9.2%) and 10 (6.6%) patients in the LV- and RV-stimulation groups, respectively (p=0.40). All but one patient (in the RV-stimulation group) were treated with a Sapien 3 valve (99.7%).

Primary endpoint

With respect to the primary endpoint analysis, procedure duration was available for all patients in the LV-stimulation group and all but one (0.7%) patient in the RV-stimulation group. Mean procedure duration was significantly shorter in the LV-stimulation group compared with the RV-stimulation group: 48.4 ± 16.9 min vs. 55.6 ± 26.9 min, p=0.0013 (Central Illustration), with an absolute difference of -0.12 (95% CI -0.20 to -0.05) in the log transformed procedure duration (p=0.0012) (Table 2).

Secondary endpoints

(i) Efficacy of stimulation

Data regarding efficacy of stimulation was available for 293 (96.7%) patients. Effective stimulation was achieved in a similar proportion of patients in both groups: 124/145 (84.9%) patients in the direct LV-stimulation group compared with 128/145 (87.1%) in the RV-stimulation group (absolute difference -2.14, 95% confidence interval [CI] -10.09 to 5.80, p=0.60) (Table 2).

Of all temporary pacemaker leads used in the RV-stimulation group, 75 (49.7%) were balloon catheters. In the LV-stimulation group, bailout placement of a right ventricular temporary pacing lead because of intraprocedural conduction disturbance (new-onset left bundle branch block or atrio-ventricular block) was done in 14 (9.3%) patients, whereas in the RV-stimulation group, the temporary pacing lead was left in situ after the procedure because of a conduction disturbance in 38 (25.0%) patients (p<0.001). There was no significant difference in rates of permanent pacemaker implantation within 30 days post-procedure between the LV- and RV-
stimulation groups: 27 (17.9%) vs. 18 (11.8%) patients, respectively (p=0.14). Pacemaker implantation was done at a mean of 3 days post-procedure.

(ii) Safety of stimulation

Procedural success was also similar in both groups: 151 (100%) patients in the LV-stimulation group and 151 (99.3%) in the RV-stimulation group (absolute difference 0.66, 95% CI -0.63 to 1.94, p=0.99) (Table 2).

Clinical follow-up at 30 days was available in 301 (99.3%) patients. Clinical outcomes are shown in Table 3. At 30 days, rates of MACE-TAVI did not significantly differ between the groups: 21 (13.9%) vs. 26 (17.1%) (p=0.44) (Figure 2). There was no significant difference in the individual components of MACE-TAVI between treatment groups: all-cause mortality occurred in 4 (2.6%) vs. 6 (3.9%) patients (p=0.75); a major cerebrovascular event occurred in 5 (3.3%) vs. 9 (5.9%) patients (p=0.41); myocardial infarction occurred in 0 (0%) vs. 1 (0.7%) patients (p=0.99); cardiac tamponade occurred in 2 (1.3%) vs. 4 (2.6%) patients (p=0.68); a bleeding event occurred in 7 (4.6%) vs. 7 (4.6%) patients (p=0.99); and vascular complications occurred in 9 (6.0%) vs. 10 (6.6%) patients (p=0.99) in the LV- and RV-stimulation groups, respectively.

The mean cumulative fluoroscopy time was significantly lower in the LV-stimulation compared with RV-stimulation group (13.48 ± 5.98 vs. 14.60 ± 5.59, respectively, absolute difference -1.12 95% CI -2.43;0.20, p=0.02). The mean absorbed radiation dose (Air Kerma) (353.4 ± 257.9 vs. 375.6 ± 255.3 mGy, absolute difference -20.2 mGy, 95% CI -78.4 to 38.0, p=0.39) and mean dose area product (35.2 ± 25.8 vs. 31.2 ± 25.2 Gy.cm², absolute difference 3.28, 95% CI -2.48 to 9.05, p=0.34) were similar in both treatment groups. Procedural fluoroscopy time and radiation dose are shown in Table 2.

(iii) Length of hospital stay and cost
There was no significant difference in length of hospital stay between the treatment groups (5.55 ± 3.35 vs. 5.85 ± 3.87, p=0.48) (Online table 4). LV-stimulation was associated with significantly lower overall costs at 30 days compared with RV-stimulation (€18,807 ± €1,318 vs. €19,437 ± €2,318, respectively, absolute difference €630, p=0.001). Procedural costs were significantly lower with LV- compared with RV-stimulation (€15,048 ± €303 vs. €15,576 ± €1,661, absolute difference €528, p<0.001), while costs of the index hospitalization and re-hospitalization did not significantly differ between the treatment groups. Mean costs per patient at 30 days are shown in Online table 5. Costs weights for procedural materials and catheterization lab time are shown in Online table 6.

DISCUSSION

The main findings of the EASY-TAVI trial were that use of the valve delivery guidewire in the left ventricle for rapid ventricular pacing during TAVI with a SAPIEN 3 valve was associated with a significantly reduced procedure duration, fluoroscopy time, and cost compared with use of a standard temporary pacing lead in the right ventricle, with similar efficacy and safety.

Standard temporary pacing leads have a rigid electrode at the distal tip, which is associated with a risk of myocardial perforation.(17) Although use of smaller (4 or 5 French), balloon-tip pacing leads may be less traumatic, these are generally softer than larger catheters and tend to be more difficult to position, thus increasing procedure duration and fluoroscopy time. They also tend to be less stable, with more frequent loss of capture during pacing. If this were to occur during valve deployment, it would carry a risk of valve misplacement or embolization, with potentially devastating consequences. In the FRANCE-2 and FRANCE-TAVI registries, for example, valve migration occurred in 1.3% and 1.1% of cases, respectively.(18) Although a soft-tipped active fixation temporary pacing lead (Tempo Lead, BioTrace Medical, San Carlos, CA, USA) that aims to decrease the risk of trauma and
increase pacing stability has received both European CE mark certification (May 2019) and U.S. FDA approval (October 2016) for use in cardiac procedures requiring pacing,(17,19) the device has not yet been evaluated in a randomized clinical trial and will likely further increase procedural cost compared with a standard temporary pacing lead.

Single-arm studies have previously shown rapid ventricular pacing via the left ventricular guidewire during TAVI to be safe, effective, reproducible, and well-tolerated by patients.(8,9) EASY-TAVI represents the first randomized study to compare this technique with conventional RV-stimulation using a temporary pacing lead. LV-stimulation was found to be as effective as RV-stimulation and some advantages over standard temporary pacing were confirmed. By obviating the need for a temporary pacing wire, LV-stimulation allows further simplification of the TAVI procedure and offers a less invasive technique, thereby reducing procedure duration, fluoroscopy time, and cost, as observed in our study, and potentially reducing the risk of procedural complications.

It is notable that the observed procedure durations in both groups were markedly shorter (48.4 ± 16.9 min vs. 55.6 ± 26.9 min in the LV- and RV-stimulation groups, respectively, p=0.0013) than the predicted durations (70 ± 35 vs. 80 ± 35 min, respectively). This may be explained by the fact that some time has elapsed since the studies these estimations were based on were completed, with inevitable reductions in procedure duration owing to procedure simplification and improvements in operator expertise over time.

Moreover, all centres that participated in the current study were experienced TAVI centres. While mean procedural fluoroscopy time in the LV-stimulation group was significantly lower compared with the RV-stimulation group, this did not translate into a lower mean procedural radiation dose. Finally, the reduced cost at 30 days observed with LV- compared with RV-stimulation was due to a significant reduction in procedural cost, due to a reduction in both the cost of materials and catheterization lab time.
While no significant reduction in procedural complications or improvement in clinical outcomes was observed, the study was not powered to show such differences. The numerically lower rates of vascular complications and cardiac tamponade in the LV-stimulation group are reassuring, however. Vascular complications occurred in 6.0% vs. 6.6% in the LV- and RV-stimulation groups, respectively (p=0.99). These rates compare favorably with those in the SAPIEN 3 group in the PARTNER 3 trial (6.5%) and in the SAPIEN XT group in the transfemoral cohort of the PARTNER 2A trial (8.5%) and in the CHOICE trial (14%).(20-22) Cardiac tamponade occurred in 1.3% of the LV-stimulation group compared with 2.6% of the RV-stimulation group (p=0.68). No case was attributed to the guidewire in the LV-stimulation group, whereas two of the four cases in the RV-stimulation group were attributed to the temporary pacing lead. The remaining cases in both groups were caused by annulus rupture. While rates of cardiac tamponade are not consistently reported in randomized trials or registries, a large-scale national TAVI registry in France (n=12,804) recently reported a significant increase in tamponade rates over time from 1.3% in the period 2010-2012 to 2.0% in the period 2013-2015 (p=0.004), with no difference according to valve type (Edwards SAPIEN or Corevalve).(18) No data was provided on the proportion of cases that were attributed to the temporary pacing lead, however. In a smaller, single-center study of cardiac tamponade during TAVI, the rate of tamponade (4.3%) observed was markedly higher, with half of cases being attributed to right ventricular perforation by the temporary pacemaker lead,(23) although two thirds of these cases were caused by either active fixation or epicardial leads.

LV-stimulation eliminated the need for a transvenous temporary pacing lead in the majority of cases: bailout placement of a right ventricular temporary pacemaker lead because of conduction disturbances was done in only 9.3% of patients in the LV-stimulation group. In contrast, in the RV-stimulation group, the temporary pacing lead was left in situ post-
procedure in one quarter of cases, despite similar rates of pre-existing conduction disturbances and ultimately, similar rates of permanent pacemaker implantation in both groups. This would seem to indicate a lower threshold for an in-dwelling temporary pacing lead post-procedure when there is already one in place. However, this is inconvenient for the patient and increases the risk of adverse events, including infection and thromboembolism – either related to the pacing lead or to deep vein thrombosis due to delayed ambulation post-procedure. These outcomes were not assessed in the current study. The rate of pacemaker implantation in our study was 14.9%, which is broadly consistent with that seen in patients treated with the SAPIEN 3 and XT valves in randomized trials. In patients treated with the SAPIEN 3 valve, rates of pacemaker implantation range from 6.5% in the PARTNER 3 trial to 19% in the SOLVE TAVI trial,(20,24) depending on the patient risk profile. In patients treated with the SAPIEN XT valve, rates vary from 6.8% in PARTNER 2B to 8.5% in PARTNER 2A to 17.3% in the CHOICE trial.(3,21,22)

On the basis of our data it might be reasonable to recommend the following approach for temporary pacing during TAVI implantation: if risk factors for development of high-grade conduction disturbances are present, upfront RV-stimulation with a temporary pacing lead should be considered; otherwise LV-stimulation might be used. According to previous observational studies, baseline predictors of development of high-grade atrio-ventricular block and the need for permanent pacing include pre-existing conduction disturbances such as right bundle branch block, first degree atrio-ventricular block, and left anterior hemiblock,(25) and anatomical factors such as heavy calcification of the left ventricular outflow tract.(26) On the other hand, should high-grade intraprocedural conduction disturbances develop in patients who undergo an initial strategy of LV-stimulation, a temporary pacing lead should be inserted at the end of the procedure. Use of LV-stimulation in TAVI is particularly attractive in patients with an in-dwelling permanent pacemaker to
avoid the risk of pacemaker lead dislodgement with a temporary pacing lead. This technique may also be useful in transcatheter heart valve implantation in the mitral position and in transcatheter tricuspid valve interventions, where having a standard temporary pacing lead across the tricuspid valve may interfere with the procedure.

The multicenter nature of this study – which was conducted at ten sites – increases the external validity of the findings. However, a number of important limitations should be considered when interpreting the results. First, the study was not powered to show differences with respect to clinical outcomes. A larger randomized study would be needed to confirm or refute such differences. Second, the results apply only to the Edward SAPIEN valve studied. The benefit of LV-stimulation may be less with self-expanding valves due to the significantly higher incidence of conduction disturbances requiring permanent pacemaker implantation post-procedure. (22,24,27) Finally, our finding are applicable to patients at intermediate predicted risk of surgical mortality, given that the mean STS score and logistic EUROSCORE were 4.8% and 13.0%, respectively. However, we feel that the results are generalizable to the classical patient at high predicted risk of surgical mortality undergoing TAVI. Such patients tend to have higher rates of co-morbidities, including peripheral vascular disease, placing them at higher risk of vascular complications and tend to have thinner RV walls, placing them at higher risk of RV-perforation using a conventional temporary pacing wire. In addition, as we begin to treat even lower risk patients, (20,28,29) we feel the results are also relevant as such patients are likely to have lower rates of pre-existing conduction abnormalities associated with increased risk of developing atrioventricular block requiring post-procedural RV-pacing.

CONCLUSIONS

In patients undergoing TAVI with a SAPIEN 3 valve, rapid ventricular pacing via a guidewire in the left ventricle significantly reduced procedure duration, fluoroscopy time, and
cost compared with right ventricular stimulation with a standard temporary pacing wire, while maintaining efficacy and safety. By eliminating the need for a transvenous temporary pacing lead or additional venous access in the majority of cases, left ventricular pacing succeeded in simplifying the TAVI procedure.

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PERSPECTIVES

WHAT IS KNOWN?

Rapid ventricular pacing is necessary to ensure transient cardiac standstill during TAVI. However, placement of a transvenous temporary pacing lead in the right ventricular apex increases procedural risk, by increasing the risk of vascular complications or right ventricular perforation, in addition to increasing procedure duration, fluoroscopy use, and cost.

WHAT IS NEW?

We showed that rapid ventricular pacing using the 0.035” guidewire in the left ventricle obviates the need for a transvenous temporary pacing lead or additional venous access in the majority of cases, thereby simplifying the TAVI procedure and significantly reducing procedure duration, fluoroscopy time and cost compared with standard RV-pacing.

WHAT IS NEXT?

A larger randomized study would be needed to investigate whether LV-stimulation is associated with improved clinical outcomes compared with RV-stimulation.
REFERENCES


29. FDA. FDA expands indication for several transcatheter heart valves to patients at low risk for death or major complications associated with open-heart surgery. 2019.
FIGURE LEGENDS

Figure 1. Study flowchart
LV-stimulation = left ventricular stimulation; mITT = modified intention-to-treat; RV-stimulation = right ventricular stimulation; TAVI = transcatheter aortic valve implantation

Figure 2. Kaplan-Meier curves showing MACE-free survival at one month
LV-stimulation = left ventricular stimulation; MACE = major adverse cardiac events; RV-stimulation = right ventricular stimulation

Central Illustration. Procedure duration in both treatment groups
LV-stimulation = left ventricular stimulation; RV-stimulation = right ventricular stimulation
The error bars indicate the upper standard deviation of the mean procedure duration for both treatment groups.
Table 1. Baseline patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>LV-stimulation (n=151)</th>
<th>RV-stimulation (n=152)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>82.70 (5.71)</td>
<td>83.18 (5.52)</td>
</tr>
<tr>
<td>Age ≥65 years</td>
<td>148 (98.0%)</td>
<td>151 (99.3%)</td>
</tr>
<tr>
<td>Female sex</td>
<td>80 (53.0%)</td>
<td>70 (46.1%)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.9 (22.7-29.7)</td>
<td>26.5 (23.3-29.1)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>121 (80.1%)</td>
<td>121 (79.6%)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>13 (8.6%)</td>
<td>11 (7.2%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>38 (25.2%)</td>
<td>30 (19.7%)</td>
</tr>
<tr>
<td>- Insulin-dependent</td>
<td>11 (28.9%)</td>
<td>12 (40.0%)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>66 (43.7%)</td>
<td>77 (50.7%)</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>47 (31.1%)</td>
<td>54 (35.5%)</td>
</tr>
<tr>
<td>Previous CAGB</td>
<td>5 (3.3%)</td>
<td>12 (7.9%)</td>
</tr>
<tr>
<td>Previous cardiac valve surgery*</td>
<td>3 (2.0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Respiratory insufficiency</td>
<td>15 (9.9%)</td>
<td>19 (12.5%)</td>
</tr>
<tr>
<td>PAD</td>
<td>18 (11.9%)</td>
<td>25 (16.4%)</td>
</tr>
<tr>
<td>Previous TIA or stroke</td>
<td>19 (12.6%)</td>
<td>10 (6.6%)</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>74 (49.0%)</td>
<td>73 (48.0%)</td>
</tr>
<tr>
<td>- Hemodialysis</td>
<td>1 (0.7%)</td>
<td>4 (2.6%)</td>
</tr>
<tr>
<td>Pacemaker in situ</td>
<td>12 (7.9%)</td>
<td>8 (5.3%)</td>
</tr>
<tr>
<td>Severely reduced mobility</td>
<td>6 (4.0%)</td>
<td>6 (3.9%)</td>
</tr>
<tr>
<td>Critical pre-operative state</td>
<td>10 (6.6%)</td>
<td>9 (5.9%)</td>
</tr>
<tr>
<td>Logistic EuroSCORE (%)</td>
<td>12.72 (9.96)</td>
<td>13.25 (10.14)</td>
</tr>
<tr>
<td>STS score (%)</td>
<td>4.93 (5.49)</td>
<td>4.76 (4.12)</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Dyspnea</td>
<td>149 (98.7%)</td>
<td>150 (98.7%)</td>
</tr>
<tr>
<td>- Syncope</td>
<td>147 (97.4%)</td>
<td>149 (98.0%)</td>
</tr>
<tr>
<td>- Angina (CCS class IV)</td>
<td>5 (3.3%)</td>
<td>13 (8.6%)</td>
</tr>
<tr>
<td>Principal indication for TAVI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Frailty</td>
<td>90 (59.6%)</td>
<td>93 (61.2%)</td>
</tr>
<tr>
<td>- High operative risk</td>
<td>38 (25.2%)</td>
<td>41 (27.0%)</td>
</tr>
<tr>
<td>- Technical contra-indication to surgery</td>
<td>18 (11.9%)</td>
<td>16 (10.5%)</td>
</tr>
<tr>
<td>- Other</td>
<td>5 (3.3%)</td>
<td>2 (1.3%)</td>
</tr>
</tbody>
</table>

| Aortic valve mean gradient (mmHg)† | 47.54 (13.65) | 48.86 (13.78) |
| Aortic valve area (cm²)† | 0.74 (0.19) | 0.73 (0.21) |
| Bicuspid aortic valve† | 7/145 (4.8%) | 10/151 (6.6%) |
| LVEF† | 57.91 (13.38) | 60.25 (11.35) |

| Pre-existing conduction disturbance‡ | 11/126 (8.7%) | 16/131 (12.2%) |
| - First degree AV-block | 6/126 (4.8%) | 12/131 (9.2%) |
| - Left bundle-branch block | 4/126 (3.2%) | 7/131 (5.3%) |

Data are shown as mean (SD), number (%) or n/N (%).
AV = atrio-ventricular; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CCS = Canadian cardiac society; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PAD = Peripheral artery disease; PCI = percutaneous coronary intervention; STS = society of thoracic surgeons; TAVI = transcatheter aortic valve implantation; TIA = transient ischemic attack
* Mitral valve replacement accounted for all cases of previous valve surgery.
† Echocardiography data was available for 296 (97.7%) patients.
‡ Preprocedural electrocardiogram data was available for 257 (84.8%) patients.
### Table 2. Procedural outcomes

<table>
<thead>
<tr>
<th></th>
<th>LV-stimulation (N=151)</th>
<th>RV-stimulation (N=152)</th>
<th>Absolute difference [95% CI]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural success</td>
<td>151.00 (100%)</td>
<td>151.00 (99.3%)</td>
<td>0.66%, 95% CI -0.63% to 1.94%</td>
<td>0.99</td>
</tr>
<tr>
<td>Procedure duration (min)*</td>
<td>48.40 (16.9)</td>
<td>55.60 (26.9)</td>
<td>-</td>
<td>0.0013</td>
</tr>
<tr>
<td>Procedure duration (min)</td>
<td>3.83 (0.32)</td>
<td>3.95 (0.34)</td>
<td>-0.12 (95% CI -0.20 to -0.05)</td>
<td>0.0012</td>
</tr>
<tr>
<td>Efficacy of stimulation</td>
<td>124.00 (84.9%)</td>
<td>128.00 (87.1%)</td>
<td>-2.1% (95% CI -10.09% to 5.80%)</td>
<td>0.60</td>
</tr>
<tr>
<td>Fluoroscopy time (min)†</td>
<td>13.48 (5.98)</td>
<td>14.60 (5.59)</td>
<td>-1.12 (95% CI -2.43 to 0.20)</td>
<td>0.02</td>
</tr>
<tr>
<td>Fluoroscopy time (min)</td>
<td>2.52 (0.40)</td>
<td>2.62 (0.36)</td>
<td>-0.10 (95% CI -0.18 to -0.01)</td>
<td>0.03</td>
</tr>
<tr>
<td>Total radiation dose – AIR Kerma (mGy)†</td>
<td>355.35 (257.88)</td>
<td>375.55 (255.27)</td>
<td>-20.20 (95% CI -78.41 to 38.01)</td>
<td>0.40</td>
</tr>
<tr>
<td>Total radiation dose – dose surface area (Gy.cm²)</td>
<td>35.16 (25.79)</td>
<td>31.87 (25.18)</td>
<td>3.28 (95% CI -2.48 to 9.05)</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Data are shown as mean (SD), number (%).
The absolute difference corresponds to a difference in means for continuous variables and to a difference in percentages for categorical variables.

*Data was available for 302 (99.7%) patients.
†Data was available for 301 (99.3%) patients.
<table>
<thead>
<tr>
<th></th>
<th>LV-stimulation (N=151)</th>
<th>RV-stimulation (N=152)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE TAVI</td>
<td>21 (13.9%)</td>
<td>26 (17.1%)</td>
<td>0.44</td>
</tr>
<tr>
<td>All-cause death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>4 (2.6%)</td>
<td>6 (3.9%)</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>3 (2.0%)</td>
<td>4 (2.6%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Major cerebrovascular event</td>
<td>5 (3.3%)</td>
<td>9 (5.9%)</td>
<td>0.41</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0 (0%)</td>
<td>1 (0.7%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caused by temporary pacing lead</td>
<td>2 (1.3%)</td>
<td>4 (2.6%)</td>
<td>0.68</td>
</tr>
<tr>
<td>Caused by annulus rupture</td>
<td>0 (0%)</td>
<td>2 (1.3%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 (1.3%)</td>
<td>2 (1.3%)</td>
<td></td>
</tr>
<tr>
<td>Bleeding</td>
<td>7 (4.6%)</td>
<td>7 (4.6%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Vascular complication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major*</td>
<td>9 (6.0%)</td>
<td>10 (6.6%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Minor*</td>
<td>2/150 (1.3%)</td>
<td>3 (2.0%)</td>
<td></td>
</tr>
<tr>
<td>Arterial</td>
<td>6/150 (4.0%)</td>
<td>7 (4.6%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>7 (4.6%)</td>
<td>10 (6.6%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 (1.3%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Other major cardiovascular event†</td>
<td>8 (5.3%)</td>
<td>2 (1.3%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Pacemaker implantation</td>
<td>27 (17.9%)</td>
<td>18 (11.8%)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Data are shown as number (%) or n/N (%).
*Data regarding severity of vascular complication was missing for one patient in the LV-stimulation group.
† Other major cardiovascular events are described in Online table 7.
Procedure duration (mins)

LV-stimulation: 48.4 minutes
RV-stimulation: 55.6 minutes

p = 0.0013
307 patients randomised

4 patients excluded from mITT analysis
- 1 patient did not undergo TAVI
- 3 patients received a valve other than Edward Sapien 3 or XT

303 patients included in mITT analysis

LV-stimulation (n=151)

Clinical follow-up at 30 days
150 (99.3%) patients completed follow-up or died

151 patients included in mITT analysis

RV-stimulation (n=152)

Clinical follow-up at 30 days
151 (99.3%) patients completed follow-up or died

152 patients included in mITT analysis